2 August 2016

Cover Sheet for Wake Therapy Protocol (IRB #7316R)

Overview: This outline is a guide for you to use while considering whether to participate in this research study. The consent that follows includes much more information about the study and its risks, which you will need to make a decision. Please read this outline and the consent carefully, and only sign it if you are comfortable doing so.

- You are being asked to participate in a research treatment study because you are depressed and have bipolar disorder.
- You must not be taking an antidepressant medication.
- You will first be treated with lithium if you are not already taking it. You will complete daily sleep, mood and activity logs for two weeks.
- You will then return and be re-evaluated. If you are no longer depressed or otherwise no longer meet study requirements, you will not continue the remainder of the study, but will be offered six months of treatment.
- If you remain depressed at re-evaluation, you will come into the hospital and begin Wake Therapy (not sleeping for approximately 36 hours) and Light Therapy (simulating sun light).

Type of treatment: This study will last about eight weeks, including two pre-hospital weeks, a week in the hospital and five post-hospital weeks. During the week in the hospital, you will remain awake for three nonconsecutive nights, sleeping and using light treatment at specified times. After leaving the hospital, you will continue sleeping and light therapy at specified times for five weeks. After the five post-hospital weeks, your study doctor will continue to see and treat you at least monthly, continuing light therapy and lithium if it was helpful and trying other treatments if not. Until the end of the post hospital five weeks, the Depression Evaluation Service and the New York State Psychiatric Institute will provide a light box for the light therapy, lithium and modafinil (Provigil®) should you need it to stay awake in the hospital. Should you need other medication at any time, or decide to continue lithium and/or light therapy following the five week post-hospital period, your study doctor will write prescriptions but the Depression Evaluation Service and the New York State Psychiatric Institute cannot provide or pay for these. Unless you require hospitalization, you will be an outpatient except for the week the study requires you to be in the hospital. After the six months of follow-up treatment, your study doctor will make referrals as seem most appropriate for your continued care.

Alternatives to participation: You do not have to participate in this research study to receive treatment for depression. If you decide not to participate, the doctor who evaluated you will help you find an alternative.

Risks: There are risks and discomforts associated with participating in this study (please read the "Risks" section of the detailed consent for a complete listing and explanation of risks). These include:

- Your depression may not improve.
- Lithium can cause trouble thinking, clumsiness, shaking, nausea, and loose bowels. In addition, too much lithium can be dangerous, so your blood will be drawn to see how much lithium is in it and your lithium dose will be changed so a preset amount is in the blood. Also, when too much is in your blood, lithium is thought to damage the kidney so we will also use some of the blood samples to test how your kidneys are working.
- Bright light can over-stimulate some people and bipolar patients may become hypomanic or manic.
- Missing sleep can also over-stimulate and induce switching from depression to mania or hypomania.

Compensation: None

Voluntary Participation: Participation in this study is entirely voluntary. You do not have to participate if you do not want to and can stop participating at any time.

CONSENT FORM

Combined wake therapy, light therapy and lithium for bipolar depression

Purpose and Overview

The purpose of this study is to find out whether the combination of keeping people awake (wake therapy), light therapy (sitting in front of a bright light) and lithium helps depression. You are being asked to participate in this study because you are depressed and have mood swings (bipolar disorder).

Voluntary

Participation in this research study is voluntary. If you decide not to participate, or if you later decide to stop participating, you will not lose any benefits to which you are otherwise entitled. A decision not to participate or withdraw your participation will not affect your current or future treatment at the New York State Psychiatric Institute or Columbia University.

Alternatives to Participation

Your participation in this study is voluntary and there are alternatives. If you previously participated in another treatment study, you may be eligible for further treatment without taking part in this study. You can go to a private doctor or to a psychiatry clinic where you may receive any of the medications marketed for depression. Electroconvulsive treatment and focused psychotherapy are also accepted treatments for depression. Electrical stimulation of a nerve in the neck (called the vagus nerve) has also been approved by the FDA.

Study Procedures

In order to find out if you can be treated in this study, you will receive a complete psychiatric evaluation by a study psychiatrist. If the study psychiatrist decides you can participate, you will be given this consent form to read. If you then agree to participate and are satisfied that your questions have been answered, you will then sign the consent form. A member of the research team will then complete research rating forms, you will complete self-report ratings, blood will be drawn for routine laboratory testing (for example, to make sure your kidneys and liver are healthy), a doctor will perform a physical examination (for example, listen to your heart and lungs, look into your eyes) and you will provide a urine specimen (to be checked for kidney function, pregnancy if you are a woman of child-bearing age, and street drugs such as heroin and cocaine). These tests will determine if you have a medical disorder such as low thyroid function that might be the cause of your depression or that should be treated prior to your entry into this study or might make one of the study medications unsafe. If you have one of these medical problems, your doctor will discuss this with you at the first visit after it is found, or telephone you if it requires quicker attention.

You have been offered participation in this study because you have bipolar disorder (that is, you have a history of feeling too good, sometimes called “high”, and at other times feeling sad or low). If you are taking a mood stabilizer (such as lithium, carbamazepine [Tegretol®] or valproex [Depakote®]), you may continue it if it seems helpful. The study, however, requires that you take lithium and that a specific amount

of lithium be in your blood; therefore, if you are already taking lithium, a blood level will determine whether your doctor needs to adjust the dose. If you are not already taking lithium, your study doctor will begin it and adjust the dose according to how much is in your blood. If you require hospitalization due to your depression or you become manic and need to be hospitalized, lithium can be started or continued in the hospital.

Once your lithium level has been adjusted, you will keep a log of your mood, energy and sleep for two weeks (one week can be retrospective). If you are not depressed after lithium adjustment and/or after the one or two weeks of keeping a log, you will not enter the hospital and not continue in the study, although your study doctor will remain responsible for your care for six months, if you so desire. If you remain depressed, your lithium level is in the required range) and you otherwise remain eligible and do not withdraw your consent, you will enter the hospital for a week (six full days plus parts of the first and last days). After the first night in the hospital, you will stay awake the entire next night by engaging in continuous activity. A medication to help you maintain wakefulness (modafinil [Provigil®] will be available to you but you are not required to take it. If you decide to use modafinil and still have trouble remaining awake the dose can be increased. If you have certain problems with your heart, you should not take modafinil and will not be able to participate in this study. The morning after remaining awake all night and thereafter you will sit for up to an hour in front of a bright light at a time determined by when you want to be asleep and awake. These sleep and wake times will also determine when you will be allowed to sleep. Day 3 you will remain awake again for an entire night, again followed by sleep at a predetermined time, and then (Day 5) have a third night of complete wakefulness. During times you are scheduled to be awake, you will be asked to enter information into a computer as evidence of your being awake. After one week, if your clinical state requires further hospitalization, you may be asked to stay—otherwise, you will be discharged. Except for patients who require hospitalization, the reason for being in the hospital is to make sure you do not fall asleep at all during the prescribed times of wakefulness and to observe your initial response to treatment. Your blood will be drawn to determine how much lithium is in it, and your lithium dose may be changed and subsequent blood drawn for determination of its lithium content until the amount in your blood is within the range generally thought to be most effective.

Your hospital stay will be on an inpatient unit of the New York State Psychiatric Institute, where you will be assigned a bed in a private or semi-private room (i.e., with a room-mate). The unit has daily routines that include a variety of activities, including group therapy, recreational activities and other types of groups, such as learning life skills. You do not have to participate in these activities but are invited to join any you like. The unit staff includes doctors, nurses, social workers and aides, all of whom will be available to you. In addition, study staff from the Depression Evaluation Service will come to the unit to ask you questions about how you are doing and to adjust the timing and duration of your sleep and use of lights and adjust the dose or change your medication. It is the patient's right to withdraw from the study at any time.

Following the completion of the three nights of wake therapy over one week, study visits will occur weekly for five weeks, whether or not you remain in the hospital. At these visits you will be asked standard

questions about the symptoms common to depression and mania, and if you are taking lithium, blood will be drawn periodically to check your lithium level and your lithium dose adjusted if necessary. In addition, throughout you will complete a daily log of your sleep-wake pattern, mood and energy levels, and the time of day you use the light. The timing and duration of your use of light therapy will be adjusted based on these logs.

Once the six week treatment study is completed, you will have the option of continuing this treatment if it has been sufficiently helpful, or to try other treatments if not. If you want to continue light therapy, you will have to purchase your own light box (cost approximately $160), although during the six weeks, a light box and the lithium will be provided to you. Whether you continue the study treatment or not, the treating staff will be available to continue your treatment for an additional six months, but you will have to pay for any medication during this six months. At the six monthly visits you will complete the same ratings as during the first six weeks.

Risks and Inconveniences

General. A general risk is that you may remain depressed. It has not been determined whether the combination of wake therapy, light therapy and lithium is effective for your disorder. Second, suicide is a risk in patients who are depressed, and those with bipolar disorder may become manic. These risks will be minimized by: (a) hospitalization of patients who enter the study while suicidal; (b) continuing hospitalization for study participants who are suicidal or manic at the completion of Wake Therapy; and (c) by weekly visits and 24 hour phone availability of an experienced research psychiatrist. Third, medication is dispensed in childproof packages, but extra precautions need to be taken to keep the medication away from children.

Wake Therapy. The major risk of Wake Therapy is mania. This possibility will be minimized by conducting wake therapy on an inpatient unit, assessing patients daily for symptoms of mania, and by retaining in the hospital patients judged to be unsafe outside the hospital. Also, as lithium is well-documented to prevent and treat mania, its institution prior to the start of Wake Therapy may help to prevent or lessen manic symptoms.

Lithium. The biggest risk in the use of lithium is toxicity, which usually occurs when there is too much lithium in the system. Symptoms of lithium toxicity include severe nausea, vomiting, severe diarrhea, mental confusion, and incoordination. As long as lithium is stopped quickly, these symptoms stop and do not progress. Therefore, you must immediately notify your study doctor if you develop severe abdominal symptoms, mental confusion or difficulty getting your hands or feet to function properly (that is, you begin to stagger, cannot tie your shoes or hit the buttons on the telephone) and not continue taking lithium until you discuss this further with him or her. Other common side effects of lithium include, nausea, loose stools, increased urination, fine hand tremor, acne, hair loss and decreased thyroid function. Lithium might cause additional side effects. All side effects lessen with lower doses and stop with discontinuation.

Light Therapy. Patients may become over-stimulated, and those with bipolar disorder may become manic. As light therapy will be started as an inpatient in a psychiatric hospital, and the researchers will be asking about manic symptoms, the development of manic symptoms or overstimulation without mania will be noted soon after its development and the light therapy dosage decreased or light therapy stopped. Light exposure may also cause headache, nausea or eye irritation, but these are uncommon. Such side effects will be counteracted by increasing the distance for the light, decreasing the time you sit at the light or discontinuing the light treatment. Long-term research studies have found that light therapy is safe for the retina of the eye. Nevertheless, as a precaution, we will examine your retina to see whether there are already signs of damage, and you will not receive light therapy if you have retinal conditions such as retinitis pigmentosa or macular degeneration. As the lights used are similar to early morning light in intensity but without any ultraviolet radiation, they may be considered safer than going outside on a sunny day.

Modafinil. While most patients tolerate modafinil well, some experience headache, nausea and nervousness. As stimulant medications, including modafinil, can cause psychotic symptoms (that is make people "crazy") and induce mania (feeling "high", "euphoric" or grandiose), should you experience symptoms such as thinking people are talking about you or following you or you hear voices when there is no one around or develop beliefs others do not share, you should let the hospital staff know immediately so they can determine whether you should continue taking modafinil and/or take a medicine to stop these symptoms. Also, if taken too close to sleep time, difficulty falling asleep may occur. Therefore, we will not give you modafinil within eight hours of your intended sleep time. Also, its use is optional, so if you wish you do not need to take it.

Additional Risks

Participation in this study may involve risks that we currently do not know.

Some discomfort may be associated with the drawing of blood samples. A maximum of 3 tablespoons of blood will be taken throughout the 6-week study. Additional small samples (about a tablespoon each time) may be needed if your lithium level needs to be changed during the 6-month follow-up period. There is a minor risk of bleeding, bruising, or infection at the site of the needle insertion.

With any treatment there is the risk that the treatment may not help and the depression might become worse. Also, if a treatment is effective or partially effective there is the risk of worsening of symptoms if the treatment is stopped or the dose is reduced.

Benefits

Your depression may improve.

You will be informed if significant new information becomes known about treatment of depression or about the treatments used in this study, especially if such information might affect the willingness of some subjects to continue their participation.

Confidentiality

All study information is kept in locked cabinets at the Depression Evaluation service at the New York State Psychiatric Institute or in a secure HIPAA compliant computer accessible only by study staff. Records will be kept confidential to the extent permitted by law. Your name and other personal identifying information will be stored in an electronically secure database at New York Psychiatric Institute. Any publications will present only group data and not include information that could identify you. *Records will be available to research staff, and to Federal, State and Institutional regulatory personnel (who may review records as part of routine audits).* Also, you should be aware that there are legal advocacy organizations that have the authority under New York State law to access otherwise confidential subject records, though they cannot re-disclose this information without the subject's consent. Electronically stored/transmitted data will be password protected with access only to study personnel.

There are limits to confidentiality. For example:

If your answers indicate a serious problem that may jeopardize your safety or health, then the researchers will contact your physician or emergency personnel as seems appropriate to your well-being. Also, suspected or known neglect or sexual or physical abuse of a child, or threatened violence to self or others will be reported to the appropriate authorities.

Study Compensation

Medications and tests that are part of the research study are provided free of charge, and neither you nor your insurance company or other third party payer will be billed for these, including hospitalization at the New York State Psychiatric Institute. Any medications or tests not required by the research will be paid for by you or your insurance company, as will any medications and light boxes used during treatment follow-up after the 6-week study.

In Case of Injury

Federal regulations require that we inform participants about our institution's policy with regard to compensation and payment for treatment of research-related injuries.

In case of injury, New York State Psychiatric Institute will provide short term emergency medical treatment, which has been determined to be necessary by New York State Psychiatric Institute's doctors, and which is within the capability of New York State Psychiatric Institute to provide. In addition, we will provide assistance in arranging follow up care in such instances.
New York State Psychiatric Institute and Research Foundation for Mental Hygiene do not provide compensation or payment for treatment of research related injuries. However, you should be aware that you do not give up your legal right to seek such compensation through the court by participating in this research.

Questions

Your study doctor will answer any questions you may have now or in the future to the best of his/her ability. If you should have additional questions, you can contact the Principal Investigator, Jonathan W. Stewart, M.D., (646-774-8070)

If you have any questions about your rights as a research participant, want to provide feedback, or have a complaint, you may call the NYSPI Institutional Review Board (IRB). (An IRB is a committee that protects the rights of human subjects in research studies). You may call the IRB Main Office at (646)774-7155 during regular office hours.

You will be notified of significant new findings that may relate to your willingness to continue to participate.

Women of Child-bearing Age

Lithium has been associated with a heart problem in children born to mothers taking lithium while pregnant. Therefore, you should not participate in this study if you are a woman of child-bearing age who might be pregnant or is unwilling to practice birth control throughout the entire study. If during the study you think you might be pregnant, you should stop lithium immediately and also immediately let your study doctor know. Prior to study entry, you will have a pregnancy test, and if it is positive, you will not be eligible for this study.

By signing this form, you are indicating that you have discussed this research study and consent form with an investigator, and he/she has answered all of your questions about the study to the best of his/her ability. Your study doctor will answer to the best of his/her ability any questions you may have about the study, your psychiatric condition or your reaction to the study procedures. If you have any further questions, you may call Jonathan W. Stewart, M.D., the Principal Investigator of this study, at 646-774-8070.

You will receive a copy of this consent form to keep.

If you have any questions about your rights as a research participant, want to provide feedback, or have a complaint, you may call the NYSPI Institutional Review Board (IRB). (An IRB is a committee that protects the rights of human subjects in research studies). You may call the IRB Executive Director at (646)774-7161 during regular office hours.

Documentation of Consent

I voluntarily agree to participate in the research study described above.

Print name: _____

Signed: _____

Date: _____

I have discussed the proposed research with this participant including the risks, benefits, and alternatives to participation (including the alternative of not participating in the research). The participant has had

an opportunity to ask questions and in my opinion is capable of freely consenting to participate in this research.

Print name: _____
Person Designated to Obtain Consent

Signed: _____

Date: _____

New York State Psychiatric Institute (NYSPI)
Authorization to Use or Disclose Health Information during a Research Study

Protocol Number: 7316R **Principal Investigator:** Jonathan W. Stewart, M.D.

Name of Study: Combined wake therapy, light therapy and lithium for bipolar depression

Before researchers can use or share any identifiable health information ("Health Information") about you as part of the above study (the "Research"), the New York State Psychiatric Institute (NYSPI) is required to obtain your authorization. You agree to allow the following individuals and entities to use and disclose Health Information about you as described below:

- New York State Psychiatric Institute (NYSPI), your doctors and other health care providers, if any, and
- The Principal Investigator and his/her staff (together "Researchers"). Researchers may include staff of NYSPI, the New York State Office of Mental Health (OMH), Research Foundation for Mental Hygiene, Inc. (RFMH), and Columbia University (CU), provided such staff is a part of the study, and
- Providers of services for the Research at CU, NYSPI and/or RFMH, such as MRI or PET, or Central Reference Laboratories (NKI), if indicated in the consent form**.**

1. The Health Information that may be used and/or disclosed for this Research includes:

☑ All information collected during the Research as told to you in the Informed Consent Form.
☐ Health Information in your clinical research record which includes the results of physical exams, medical and psychiatric history, laboratory or diagnostic tests, or Health Information relating to a particular condition that is related to the Research.
☐ Additional information may include:

2. **The Health Information listed above may be disclosed to:**

☑ Researchers and their staff at the following organizations involved with this Research:
Nathan Kline Institute (where the laboratory specimens are analyzed)

☐ The Sponsor of the Research,

and its agents and contractors (together, "Sponsor"); and

☑ Representatives of regulatory and government agencies, institutional review boards, representatives of the Researchers and their institutions to the level needed to carry out their responsibilities related to the conduct of the research.
☐ Private laboratories and other persons and organizations that analyze your health information in connection with this study

☐ Other (family members or significant others, study buddies, outside agencies etc.) Specify:

3. By giving permission to release your Health Information as described above, you understand that your Health Information may be disclosed to individuals or entities which are not required to comply with the federal and state privacy laws which govern the use and disclosure of personal Health Information by NYSPI. This means that once your Health

Information has been disclosed to a third party which does not have to follow these laws (e.g., a drug company or the Sponsor of the Research), it may no longer be protected under the HIPAA or NYS Mental Hygiene Law requirements but is subject to the terms of the consent form and may be subject to other state or federal privacy laws or regulations.

4. Please note that:

- You do not have to sign this Authorization form, but if you do not, you may not be able to participate in the study or receive study related care. You may change your mind at any time and for any reason. If you do so, you may no longer be allowed to participate in the study. If you withdraw this Authorization the research staff and the Sponsor, if this is sponsored research, may still use or disclose Health Information containing identifying information they already have collected about you as needed to maintain the reliability of the research. Any request to withdraw this Authorization must be made in writing to (enter name and contact information below):

  Jonathan W. Stewart, M.D.
  1051 Riverside Drive

- While the Research is going on, you may not be allowed to review the Health Information in your clinical research record that has been created or collected by NYSPI. When this research has been completed you may be allowed to see this information. If it is needed for your care, your Health Information will be given to you or your Doctor.

5. This Authorization does not have an end date.

6. You will be given a copy of this form after you have signed it.

I agree to the use and disclosure of Health Information about me as described above:

_____ _____

Signature of Participant/ Legal Representative Date

_____

Printed Name of Participant

_____

Relationship of Legal Representative to Participant (if applicable)

We also ask you or your legal representative to initial the statements below:

☐ **I have received a copy of the NYSPI/OMH Notice of Privacy Practices.**